

On page 2, line 14, please delete "factor-receptorcomplex" and substitute therefor --factor-receptor complex--.

On page 4, line 15, please delete "complimentary" and substitute therefor --complementary--.

Please delete all text from page 5, line 16 through page 7, line 14 and substitute therefor

1  
8

--Fig. 1 shows a characteristic fragment produced by Eco RI restriction of the cloned gene of the present invention: the restriction-site map of  $\lambda$ MAC117 and plasmid pMAC117. A: Acc I; B: Bam HI; Bg: Bgl I; N: Nco I; R: Eco RI; X: Xba I; Xh: Xho I. The sites were located by electrophoretic analysis of the products of single and double digestion. Regions homologous to v-erbB or human repetitive sequences (region flanked by arrows) were located by Southern blot hybridization (Southern, *J. Mol. Biol.* 98:503 (1975)), with the v-erbB probe or total human DNA made radioactive by nick translation (Rigby *et al.*, *J. Mol. Biol.* 113:237 (1977)). Hybridization conditions were as described in Fig. 2. The nucleotide sequence of pMAC117 between the Acc I site and the Nco I sites and regions of encoded amino acid sequence homologous to the EGF receptor are shown. The AG or GT dinucleotides flanking the putative coding regions are underlined. To determine the sequence, Nco I, Hinf I and Sau 96 I fragments were labeled at the 3' termini by means of a large fragment of *E. coli* DNA polymerase, separated into single strands by gel electrophoresis and chemically degraded (Maxam *et al.*, *Proc. Natl. Acad. Sci.*, USA 74:560 (1977)).

Fig. 2 shows the gel electrophoretic properties of specific gene fragments; detection of v-erbB- and pMAC117-specific gene fragments in normal human placenta, A431 cells or human mammary carcinoma MAC117. DNA (15 µg) was cleaved with Eco RI, separated by electrophoresis in agarose gels and transferred to nitrocellulose paper (Southern, *J. Mol. Biol.* 98:503 (1975)). Hybridization to the <sup>32</sup>P-labeled probe (Rigby *et al.*, *J. Mol. Biol.* 113:237 (1977)) was conducted in a solution of 40 percent formamide, 0.75M NaCl and 0.075M sodium citrate at 42°C (Wahl *et al.*, *Proc. Natl. Acad. Sci., USA* 76:3683 (1979)). The v-erbB probe (A) was a mixture of the 0.5-kbp Bam HI-Bam HI fragment and the 0.5-kbp Bam HI-Eco RI fragment of avian erythroblastosis proviral DNA. The pMAC117 probe (B) was a 1-kbp Bgl I-Bam HI fragment. After hybridization, the blots were washed first in 0.3M NaCl plus 0.03M sodium citrate at room temperature and then in 0.015M NaCl, 0.0015M sodium citrate and 0.1 percent sodium dodecyl sulfate at 42°C (v-erbB probed blots) or at 52°C (pMAC117 probed blots). Hybridization was detected by autoradiography.--

On page 8, after line 12 and before line 13, please insert the following: --As

disclosed in Ullrich *et al.* (1984), the nucleotide sequence of the EGF receptor gene is:

GCCGCGCTGCGCCGGAGTCCCGAGCTAGCCCCGGCGCCGCGCCGCCAGACCGGAC  
GACAGGCCACCTCGTCGGCGTCCGCCCCGAGTCCCCGCCTCGCCGCCAACGCCACAAC  
CACCGCGCACGGCCCCCTGACTCCGTCCAGTATTGA

TCGGGAGAGCCGGAGCGAGCTCTTCGGGGAGCAGCGATGCGACCCTCCGGGACGGC  
CGGGGCAGCGCTCCTGGCGCTGCTGGCTGCGCTCTGCCCGGCGAGTCGGGCTCTGGAGGAAAA

ACGCAGTTGGGCACTTTTGAAGATCATTTTCTCAGCCTCCAGAGGATGTTCAATAACT  
GTGAGGTGGTCCTTGGGAATTTGGAAATTACCTATGTGCAGAGGAATTATGATCTTT  
CCTTCTTAAAGACCATCCAGGAGGTGGCTGGTTAT

2  
GTCCTCATTGCCCTCAACACAGTGGAGCGAATTCCTTTGGAAAACCTGCAGATCATC  
AGAGGAAATATGTACTACGAAAATTCCTATGCCTTAGCAGTCTTATCTAACTATGATG  
CAAATAAAACCGGACTGAAGGAGCTGCCCATGAGA

AATTTACAGGAAATCCTGCATGGCGCCGTGCGGTTTCAGCAACAACCTGCCCTGTGC  
AACGTGGAGAGCATCCAGTGGCGGGACATAGTCAGCAGTGACTTTCTCAGCAACATG  
TCGATGGACTTCCAGAACCACCTGGGCAGCTGCCAA

AAGTGTGATCCAAGCTGTCCCAATGGGAGCTGCTGGGGTGCAGGAGAGGAGAACTG  
CCAGAAACTGACCAAAATCATCTGTGCCAGCAGTGCTCCGGGCGCTGCCGTGGCAA  
GTCCCCCAGTGACTGCTGCCACAACCAGTGTGCTGCA

GGCTGCACAGGCCCCCGGGAGAGCGACTGCCTGGTCTGCCGCAAATTCGAGACGAA  
GCCACGTGCAAGGACACCTGCCCCCACTCATGCTCTACAACCCACACGTACCAG  
ATGGATGTGAACCCCGAGGGCAAATACAGCTTTGGT

GCCACCTGCGTGAAGAAGTGTCCCCGTAATTATGTGGTGACAGATCACGGCTCGTGC  
GTCCGAGCCTGTGGGGCCGACAGCTATGAGATGGAGGAAGACGGCGTCCGCAAGTG  
TAAGAAGTGCGAAGGGCCTTGCCGCAAAGTGTGTAAC

GGAATAGGTATTGGTGAATTTAAAGACTCACTCTCCATAAATGCTACGAATATTAAA  
CACTTCAAAAACCTGCACCTCCATCAGTGGCGATCTCCACATCCTGCCGGTGGCATTTA  
GGGGTGACTCCTTCACACATACTCCTCCTCTGGAT

CCACAGGAACTGGATATTCTGAAAACCGTAAAGGAAATCACAGGGTTTTTGCTGATT  
CAGGCTTGGCCTGAAAACAGGACGGACCTCCATGCCTTTGAGAACCTAGAAATCATA  
CGCGGCAGGACCAAGCAACATGGTCAGTTTTCTCTT

GCAGTCGTCAGCCTGAACATAACATCCTTGGGATTACGCTCCCTCAAGGAGATAAGT  
GATGGAGATGTGATAATTTAGGAAACAAAAATTTGTGCTATGCAAATACAATAAAC  
TGGA AAAA ACTGTTTGGGACCTCCGGTCAGAAAACC

AAAATTATAAGCAACAGAGGTGAAAACAGCTGCAAGGCCACAGGCCAGGTCTGCCA  
TGCCTTGTGCTCCCCGAGGGCTGCTGGGGCCCGAGCCCAGGGACTGCGTCTCTTG  
CCGGAATGTCAGCCGAGGCAGGGAATGCGTGGACAAG

TGCAAGCTTCTGGAGGGTGAGCCAAGGGAGTTTGTGGAGAACTCTGAGTGCATACAG  
TGCCACCCAGAGTGCCTGCCTCAGGCCATGAACATCACCTGCACAGGACGGGGACCAGACAAC

CCCCACTGCGTCAAGACCTGCCCCGGCAGGAGTCATGGGAGAAAACAACACCCTGGTC  
TGGAAGTACGCAGACGCCGGCCATGTGTGCCACCTGTGCCATCCAACTGCACCTAC  
GGATGCACTGGGCCAGGTCTTGAAGGCTGTCCAACG

AATGGGCCTAAGATCCCGTCCATCGCCACTGGGATGGTGGGGGCCCTCCTCTTGCTG  
CTGGTGGTGGCCCTGGGGATCGGCCTCTTCATGCGAAGGCGCCACATCGTTCGGAAG  
CGCACGCTGCGGAGGCTGCTGCAGGAGAGGGAGCTT

GTGGAGCCTCTTACACCCAGTGGAGAAGCTCCCAACCAAGCTCTCTTGAGGATCTTG  
AAGGAACTGAATTCAAAAAGATCAAAGTGCTGGGCTCCGGTGCGTTCGGCACGGTG  
TATAAGGGACTCTGGATCCCAGAAGGTGAGAAAGTT

AAAATTCCCGTCGCTATCAAGGAATTAAGAGAAGCAACATCTCCGAAAGCCAACAAG  
GAAATCCTCGATGAAGCCTACGTGATGGCCAGCGTGGACAACCCCCACGTGTGCCGC  
CTGCTGGGCATCTGCCTCACCTCCACCGTGCAACTC

ATCACGCAGCTCATGCCCTTCGGCTGCCTCCTGGACTATGTCCGGGAACACAAAGAC  
AATATTGGCTCCAGTACCTGCTCAACTGGTGTGTGCAGATCGCAAAGGGCATGAAC  
TACTTGGAGGACCGTCGCTTGGTGCACCGCGACCTG

GCAGCCAGGAACGTACTGGTGAAAACACCGCAGCATGTCAAGATCACAGATTTTGGG  
CTGGCCAAACTGCTGGGTGCGGAAGAGAAAGAATACCATGCAGAAGGAGGCAAAGT  
GCCTATCAAGTGGATGGCATTGGAATCAATTTTACAC

AGAATCTATACCCACCAGAGTGATGTCTGGAGCTACGGGGTGACCGTTTGGGAGTTG  
ATGACCTTTGGATCCAAGCCATATGACGGAATCCCTGCCAGCGAGATCTCCTCCATCC  
TGGAGAAAGGAGAACGCCTCCCTCAGCCACCCATA

TGTACCATCGATGTCTACATGATCATGGTCAAGTGCTGGATGATAGACGCAGATAGT  
CGCCCAAAGTTCCGTGAGTTGATCATCGAATTCTCCAAAATGGCCCGAGACCCCCAG  
CGCTACCTTGTCATTACGGGGGATGAAAGAATGCAT

TTGCCAAGTCCTACAGACTCCAATTCTACCGTGCCCTGATGGATGAAGAAGACATG  
GACGACGTGGTGGATGCCGACGAGTACCTCATCCCACAGCAGGGCTTCTTCAGCAGC  
CCCTCCACGTCACGGACTCCCCTCCTGAGCTCTCTG

AGTGCAACCAGCAACAATTCCACCGTGGCTTGCAATTGATAGAAATGGGCTGCAAAGC  
TGTCCCATCAAGGAAGACAGCTTCTTGACGCGATACAGCTCAGACCCCACAGGCGCC  
TTGACTGAGGACAGCATAGACGACACCTTCCTCCCA

GTGCCTGAATACATAAACCAGTCCGTTCCCAAAGGCCCGCTGGCTCTGTGCAGAAT  
CCTGTCTATCACAATCAGCCTCTGAACCCCGCGCCCAGCAGAGACCCACACTACCAGGACCCCC

CTCAACACTGTCCAGCCCACCTGTGTCAACAGCACATTCGACAGCCCTGCCCCTGG  
GCCCAGAAAGGCAGCCACCAAATTAGCCTGGACAACCCTGACTACCAGCAGGACTTC  
TTTCCCAAGGAAGCCAAGCCAAATGGCATCTTTAAG

GGCTCCACAGCTGAAAATGCAGAATACCTAAGGGTCGCGCCACAAAGCAGTGAATTT  
ATTGGAGCATGACCACGGAGGATAGTATGAGCCCTAAAAATCCAGACTCTTTTCGATA  
CCCAGGACCAAGCCACAGCAGGTCTCCATCCCAAC

AGCCATGCCCGCATTAGCTCTTAGACCCACAGACTGGTTTTGCAACGTTTACACCGAC  
TAGCCAGGAAGTACTTCCACCTCGGGCACATTTTGGGAAGTTGCATTCCTTTGTCTTC  
AAACTGTGAAGCATTTACAGAAACGCATCCAGCA

AGAATATTGTCCCTTTGAGCAGAAATTTATCTTTCAAAGAGGTATATTTGAAAAAAA  
AAAAAAAAGTATATGTGAGGATTTTTATTGATTGGGGATCTTGGAGTTTTTCATTGTC  
GCTATTGATTTTTACTTCAATGGGCTCTTCCAACA

AGGAAGAAGCTTGCTGGTAGCACTTGCTACCCTGAGTTCATCCAGGCCCAACTGTGA  
GCAAGGAGCACAAAGCCACAAGTCTTCCAGAGGATGCTTGATTCCAGTGGTTCTGCTT  
CAAGGCTTCCACTGCAAAACACTAAAGATCCAAGAA

GGCCTTCATGGCCCCAGCAGGCCGGATCGGTACTGTATCAAGTCATGGCAGGTACAG  
TAGGATAAGCCACTCTGTCCCTTCCTGGGCAAAGAAGAAACGGAGGGGGATGAATTCT  
TCCTTAGACTTACTTTTGTAAAAATGTCCCCACGGT

ACTTACTCCCCACTGATGGACCAGTGGTTTCCAGTCATGAGCGTTAGACTGACTTGTT  
TGTCTTCCATTCCATTGTTTTGAAACTCAGTATGCCGCCCTGTCTTGCTGTCATGAA  
ATCAGCAAGAGAGGATGACACATCAAATAATAAC

TCGGATTCCAGCCCACATTGGATTTCATCAGCATTTGGACCAATAGCCCACAGCTGAG  
AATGTGGAATACCTAAGGATAACACCGCTTTTGTCTCGCAAAAACGTATCTCCTAAT  
TTGAGGCTCAGATGAAATGCATCAGGTCCTTTGGG

GCATAGATCAGAAGACTACAAAAATGAAGCTGCTCTGAAATCTCCTTTAGCCATCAC  
CCCAACCCCCCAAATTAGTTTGTGTTACTTATGGAAGATAGTTTTCTCCTTTTACTTC  
ACTTCAAAGCTTTTTACTCAAAGAGTATATGTT

CCCTCCAGGTCAGCTGCCCCCAAACCCCTCCTTACGCTTTGTCACACAAAAAGTGTC  
TCTGCCTTGAGTCATCTATTCAAGCACTTACAGCTCTGGCCACAACAGGGCATTTTAC  
AGGTGCGAATGACAGTAGCATTATGAGTAGTGTG



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AATTCAGGTAGTAAATATGAACTAGGGTTTGAAATTGATAATGCTTTCACAACATTT  
GCAGATGTTTTAGAAAGGAAAAAAGTTCCTTCCTAAAATAATTTCTCTACAATTGGAAGATTGGA  
TCCTAATCTGTGTGTGCCCTGTAACTGACTGGTTAACAGCAGTCCTTTGTAAACAGT  
GTTTTAACTCTCCTAGTCAATATCCACCCCATCCAATTTATCAAGGAAGAAATGGTT  
CAGAAAATATTTTCAGCCTACAGTTATGTTTCAGT

CACACACACATACAAAATGTTTCCTTTTGCTTTTAAAGTAATTTTGTACTCCAGATCA  
GTCAGAGCCCCTACAGCATTGTTAAGAAAGTATTTGATTTTGTCTCAATGAAAATAA  
AACTATATTCATTTC--

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On page 9, line 2, please delete "~~PE7~~" and substitute therefor --pE7--.

On page 9a, line 4, after "from" and before "pMAC117", please insert the  
following: --the 3' terminus of--.

On page 9a, line 1, please delete "Fig. 5" and substitute therefor --Fig. 5A--.

Please delete the following paragraph from page 22a and insert it on page 9a, at  
the end of the paragraph of the description of Fig. 5 and before the paragraph of the description of  
Fig. 6:

--Fig. 5B illustrates three probes, a, b and c, representing the 5' end, a middle portion and the entire coding region, respectively, which were employed in subsequent studies elucidating the role and function of this v-erbB-related gene.--

On page 9a, line 13, please delete "1B" and substitute therefor --5B--.

On page 9a, line 18, please delete "1B" and substitute therefor --5B--.

On page 9b, line 14, please delete "1B" and substitute therefor --5B--.

On page 9c, next to last line, please delete " $10^3$ " and substitute therefor --to  
 $10^3$ --.

On page 9d, line 3, please delete "was" and substitute therefor --were--.

Please move Table 1, which constitutes the entire page 9c, to the end of the specification (between pages 35 and 36).

On page 11, line 4, please delete "was" and substitute therefor --were--.

On page 12, line 24, please delete "nirocellulose" and substitute therefor  
--nitrocellulose--.

On page 13, line 14, please delete "1A" and substitute therefor --2A--.

On page 13, line 15, please delete "1AB" and substitute therefor --2B--.

On page 14, line 2, please delete "Hi" and substitute therefor --HI--.

On page 15, line 16, please delete "(Fig. 2)" and substitute therefor --(Fig. 1)--.

On page 15, line 20, please delete " $\alpha$ P<sup>12</sup>dXTP" and substitute therefor  
-- $\alpha$ <sup>32</sup>PdXTP--.

On page 17, line 1, please insert -- $\lambda$ -- before "MAC117".

On page 17, line 11, please delete "dithiothretol" and substitute therefor  
--dithiothreitol--.

On page 17, line 20, please delete "plaques" and substitute therefor --plates--.

On page 18, line 6, please delete "1" and substitute therefor --2--.

On page 18, line 7, please delete "Fig. 1" and substitute therefor --Fig. 2--.

On page 18, line 12, please delete the following: "To clone the 6-kbp fragment,".

On page 18, line 20, please delete "Figure 2" and substitute therefor --Figure 1--.

On page 18, line 26, please delete "Fig. 2" and substitute therefor --Fig. 1--.

On page 19, lines 8, 16 and 20, please delete "1A" and substitute therefor --2A--.

On page 19, line 12, please delete "sequamous" and substitute therefor  
--squamous--.

On page 19, line 16, please delete "framents" and substitute therefor --fragments--.

On page 20, line 5, please delete "1B" and substitute therefor --2B--.

On page 20, line 8, please delete "1A" and substitute therefor --2A--.

On page 20, line 15, please delete "(Fig. 3)" and substitute therefor --(Fig. 1)--.

On page 20, line 24, please delete "Fig. 2" and substitute therefor --Fig. 1--.

On page 21, line 16, after "probe" and before "detected", please insert the following: --, consisting of the Bgl I to Bam HI restriction fragment of pMAC117,--

On page 22a, line 2 and lines 19-20, after "Kraus et al.," and before "1987", please insert the following: --*EMBO Journal* 6:605-610,--.

On page 22a, line 4, after "from" and before "a", please insert the following: --the 3' terminus of--.

On page 22c, line 6, please delete "(Fig. 5)" and substitute therefor --(Figs. 5A,B)--.

On page 22c, line 9 and page 22d, line 16, after "DiFiore et al.," and before "1987", please insert the following: --*Science* 237:178-182,--.

On page 22c, lines 22 and 26 and on page 22d, lines 8 and 12, please delete "Table I" and substitute therefor --Table 1--.

On page 24, line 2, please delete "Figures 1" and substitute therefor --Figures 2--.

On page 24, line 28, please delete "C" and substitute therefor --c--.

On page 26, line 16, please delete "sequence of claim 4" and substitute therefor --

sequence:

2  
GlyMetSerTyrLeuGluAspValArgLeuValHisArgAspLeuAlaAlaArgAsnValLeuValLysSerProAsn  
HisValLysIleThrAspPheGlyLeuAlaArgLeuLeuAspIleAspGluThrGluTyrHisAlaAspGlyGlyLysVal  
ProIleLysTrpMetAlaLeuGluSerIleLeuArgArgArgPheThrHisGlnSerAspValTrpSerTyrGly--.

On page 26, lines 17-18, please delete "nove. v-erbB-related gene in" and  
substitute therefor --novel v-erbB-related gene is--. 13

On page 27, line 2, please delete "Figures 1" and substitute therefor --Figures 2--.

On page 27, line 5, please delete "5A" and substitute therefor --5B--.

On page 27, line 12, after "amplification" and before "of", please insert the  
following: --or increased expression--.

On page 27, line 17, after "gene" and before "are", please insert the following: --or  
its mRNA transcript--.

On page 27, line 19, please delete "Figure 1" and substitute therefor --Figure 2--.

On page 28, line 6, please delete "form" and substitute therefor --from--.

On page 28, line 7, please delete "sequence of claim 4" and substitute therefor --

sequence:

GlyMetSerTyrLeuGluAspValArgLeuValHisArgAspLeuAlaAlaArgAsnValLeuValLysSerProAsn  
HisValLysIleThrAspPheGlyLeuAlaArgLeuLeuAspIleAspGluThrGluTyrHisAlaAspGlyGlyLysVal  
ProIleLysTrpMetAlaLeuGluSerIleLeuArgArgArgPheThrHisGlnSerAspValTrpSerTyrGly--.

On page 28, line 8, please delete "described in claim 1" and substitute therefor

--having the nucleotide sequence:

GTCTACATGGGTGCTTCCCATTCCAGGGGATGAGCTACCTGGAGGATGTGCGGCTCG  
TACACAGGGACTTGGCCGCTCGGAACGTGCTGGTCAAGAGTCCCAACCATGTCAAAA  
TTACAGACTTCGGGCTGGCTCGGCTGCTGGACATTGACGAGACAGAGTACCATGCAG  
ATGGGGGCAAGGTTAGGTGAAGGACCAAGGAGCAGAGGAGGCTGGGTGGAGTGGTG  
TCTAGCCCATGGGAGAACTCTGAGTGGCCACCTCCCCACAACACACAGTTGGAGGAC  
TTCCTCTTCTGCCCTCCCAGGTGCCCATCAAGTGGATGGCGCTGGAGTCCATTCTCCG  
CCGGCGGTTACCCACCAGAGTGATGTGTGGAGTTATGGTGTGTGATGGGGGGGTGTT  
GGGAGGGGTGGGTGAGGAGCCATGG--.

On page 28, line 20, please delete "~~observations~~" and substitute therefor

--observations--.

On page 28, line 25, after "Slamon et al.," and before "1987", please insert the  
following: --*Science* 235:177-181,--.

On page 28, line 28, after "clinical", please insert --setting--.

On page 29, line 10, please delete "Figure 1" and substitute therefor --Figure 2--.

On page 30, line 1, please delete "is" and substitute therefor --are--.

On page 30, line 16, please delete "Fig. 11" and substitute therefor --Fig. 10--.

On page 31, line 5, please delete "demonstated" and substitute therefor  
--demonstrated--.

On page 31, line 6, please delete "Figure 1" and substitute therefor --Figure 2--.

On page 31, line 17, please delete "has" and substitute therefor --have--.

On page 34, line 7, please delete "instrucitons" and substitute therefor  
--instructions--.

On page 35, lines 7-8, please delete "P<sup>32</sup>" and substitute therefor --<sup>32</sup>P--.